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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/691,405	10/17/2000	Steven R. Binder	2558B-063700US	3942

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EXAMINER	
ALLEN, MARIANNE P	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 04/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/691,405	BINDER ET AL.	
	Examiner	Art Unit	
	Marianne P. Allen	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-10 and 12-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-10 and 12-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/31/05 has been entered.

Claims 1-2, 5-10, and 12-20 are under consideration.

Claim Rejections - 35 USC § 112

Claims 19-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 19-20 are not originally filed claims and basis is stated to be on page 9 for the concept of "determined simultaneously" and "substantially simultaneously." This is not agreed with. The text at this point discusses multiplexing assays for a sample. This is not the same concept as recited here. These claims are not limited to the multiplexing system of page 9 and the disclosure at page 9 does not disclose the concept or metes and bounds of "simultaneously" or "substantially simultaneously." It is not known what time frame would meet this limitation.

Claims 1-2, 5-10, and 12-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an enablement rejection.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In the instant application, a great deal of experimentation would be required that is not routine. The specification provides no direction or guidance on how to adapt known statistical pattern recognition means to solve their particular problem. There are no working examples. Computational methods of diagnosis are quite complicated such that even though the skill of those in the art is high, such inventions are difficult to develop and validate.

The specification details the difficulties in diagnosing autoimmune disorders based upon transient symptoms, overlapping symptoms, variations in normal antibody levels, and so forth. While the specification lists a variety of autoimmune diseases and lists a variety of antigens (see pages 7-8), it does not associate any antigen (or autoantibody) with any particular disease with respect to presence (or absence) and amounts. Nor does the specification disclose how discrimination between different autoimmune diseases, particularly with those that involve overlapping autoantibodies, is to be implemented. Note that none of the prior art identified by applicant concerns diagnosis of any disease using any antibody profiles and pattern recognition

means. The prior art to Grus et al. demonstrates the amount of effort required to develop such methods and all of the different decisions that must be made when determining how to solve a particular problem. Applicant has previously pointed to Cabello et al. and Tobin et al. However, Cabello et al. discloses k-nearest neighbor analysis with respect to ventricular arrhythmia detection. Cabello et al. discloses using a set of 90 ECG signal segments with specifically defined spectral parameters in the analysis and the test and learning sets are described (see at least page 78, second full paragraph, and page 83). The instant specification provides no such test sets, learning sets, or parameters. Also in contrast to the instant specification, Tobin et al. discloses a feature-based, fuzzy k-nearest neighbor classifier and optimization techniques. The classifiers and training data are disclosed. In each case, the datasets are well characterized. (See at least section 2 and 3.1.) The instant specification does not provide this type of information and how to apply it to diagnosis of systemic autoimmune diseases.

The specification provides none of this information or guidance for any aspect of the invention. Again, the specification does not associate any antigen (or autoantibody) with any particular disease with respect to presence (or absence) and amounts as implied by the claims. That is, they do not exemplify any embodiment of the claimed method. Nor does the specification disclose how discrimination between different autoimmune diseases, particularly with those that involve overlapping autoantibodies, is to be implemented. (See Thompson et al., 1993.) Finally, the breadth of the claims is broad for many aspects of the claims from the number and type of autoantibodies in the test data and library of reference data sets to the number of diseases potentially to be identified.

Note that only claims 7 and 8 specify particular antibodies to test. As written, one could practice the invention by testing for autoantibodies to microtobule organizing center (MTOC) (associated with rheumatoid arthritis) and MOG (associated with multiple sclerosis) in biological samples from a test subject and for the plurality of subjects known to have one or none of the named diseases. Executing the method by quantitating these autoantibodies would tell you nothing about whether the test subject had any of the diseases named in the preamble of the claim as these autoantibodies are not known to be associated with SLE, scleroderma, Sjogren's syndrome, polymyositis, dermatomyositis, CREST and connective tissue disease.

Although the preamble of claim 1 recites a method of identifying whether a test subject is suffering from one or more systemic autoimmune diseases, the underlying method and intent of the claims is a data mining method to discover those autoantibodies, if any, that may be statistically associated with the named autoimmune diseases and be capable of discriminating between them. That is, from the haystack of all autoantibodies (known and unknown, associated with a named autoimmune disease or not), one of ordinary skill in the art is to find the needle or collection of needles that will reveal the autoantibody profile diagnostic for a particular condition, if any such profile should exist. This is an invitation to experiment. While the specification and claims set forth a general research plan for a problem that would have been known to be of interest (and known to be complex) to those of ordinary skill in the art, the specification has not provided a solution nor sufficient guidance to enable one to find a solution. The specification proposes applying known pattern recognition means to solve a new problem. This is not a situation where new data is input into known programs for solving the problem. That is, applicant is not using known software to solve a known problem in a conventional

manner where one practicing the invention need only supply the data to be analyzed. Applicant has admitted in previous responses that the known statistical techniques will need to be adapted to solve this particular problem. However, the specification has not exemplified any method for identification within the claims nor provided guidance on the how to adapt the known statistical techniques for solving the problem of identifying systemic autoimmune disease in a subject. One of ordinary skill in the art would be required to make independent decisions and judgments on how to apply the statistical techniques, what parameters to use or change, assumptions to make, and so forth. Any model developed must be tested and validated. This is not considered to be routine experimentation. This is an invitation to experiment. It requires one of ordinary skill in the art practicing the invention to use inventive skill to develop applicant's claimed method. Again, the specification provides no training set with the information required to produce statistically derived decisions with respect to systemic autoimmune diseases. The reference data must be collected and evaluated, assumptions as to what specific data will be used must be made and the composition of the training set and test sets and so forth must be determined. The specification does not exemplify any implementation of the claimed methods and provides no specific guidance for doing so. The specification does not exemplify or identify any known library of reference data sets where "each data set [is] obtained from a biological sample of a reference subject known to have a systematic autoimmune disease of known identity." In particular, at least claims 9 and 10 require libraries of significant size (up to 2000 or 10000 biological samples) that have not been developed and thus are not available to one of ordinary skill in the art to practice the invention. At least claim 5 encompasses a test data of up to 100 autoantibodies and the specification specifically identifies less than half of that number.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne P. Allen whose telephone number is 571-272-0712. The examiner can normally be reached on Monday-Thursday, 5:30 am - 1:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Marianne P. Allen
Primary Examiner
Art Unit 1631

4/14/05

mpa